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PATENT 4518-0107PUS1

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant:

LOIBNER, Hans et al.

Conf.:

Appl. No.:

NEW

Group:

Filed:

December 23, 2004

Examiner:

For:

USE OF A PREPARATION BASED ON ANANTIBODY

DIRECTED AGAINST A TUMOR-ASSOCIATED

GLYCOSYLATION

LETTER

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450 December 23, 2004

Sir:

The PTO is requested to use the amended sheets/claims attached hereto (which correspond to Article 19 amendments or to claims attached to the International Preliminary Examination Report (Article 34)) during prosecution of the above-identified national phase PCT application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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LRS/lmt 4518-0107PUS1

Attachment(s)

Claims:

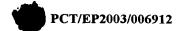
- 1. The use of a preparation based on an antibody directed against a tumor-associated glycosylation for preparing a medicament for the prophylactic and/or therapeutic treatment for the reduction or inhibition, respectively, of the growth of tumor cells in a cancer patient by inhibiting glycosylated tumor cell receptors.
- 2. The use according to claim 1 for treating a patient in combination with a chemotherapy.
- 3. The use according to claim 1 for treating a chemotherapy-resistance.
- 4. The use according to claim 1 for treating the "minimal residual disease".
- 5. The use according to any one of claims 1 to 4 for preventing the mitogenic stimulation of a tumor cell by the epidermal growth factor (EGF) and/or by heregulin.
- 6. The use according to any one of claims 1 to 5 for the lysis of tumor cells which express a receptor from the family of the EGF receptors.
- 7. The use according to any one of claims 1 to 6, characterised in that an antibody is directed against Lewis antigens.
- 8. The use according to any one of claims 1 to 7, characterised in that an antibody directed against an aberrant glycosylation is used, like Lewis x-, Lewis b- and Lewis-y-structures, as well as sialyl-Tn, Tn antigen, GloboH, KH1, TF antigen and alpha-1,3-galactosyl epitope.
- 9. The use according to any one of claims 1 to 8, characterised in that the antibody is a monoclonal antibody, in particular a human, humanized, chimeric or murine antibody.
- 10. The use according to any one of claims 1 to 9, character-

ised in that an antibody having an affinity to binding the EGF receptor with a dissociation constant of below a Kd value of 10^{-6} mol/l, preferably less than 10^{-7} mol/l, most preferred 10^{-6} mol/l, or less, is used.

- 11. The use according to any one of claims 1 to 10, characterised in that the antibody is used in a dose of at least 50 mg, preferably at least 100 mg, most preferred at least 200 mg, up to 2 g per patient.
- 12. The use according to any one of claims 1 to 11, characterised in that an antibody derivative is used which comprises at least the Fab-portion of an antibody and binds to a tumor-associated glycosylation.
- 13. The use according to any one of claims 1 to 12, characterised in that the patient suffers from a cancer with tumor cells which express a receptor from the family of the EGF receptors.
- 14. A pharmaceutical preparation for treating cancer patients and containing an antibody directed against a tumor-associated glycosylation at a concentration ranging from 0.1-10%, preferably 1-5%.
- 15. A preparation for the pharmaceutical and/or diagnostic use, based on an antibody derivative comprising at least a Fabportion of an antibody which binds to a tumor-associated glycosylation and has a CDC and ADCC activity of less than 50% of the native antibody.
- 16. The use according to any one of claims 1 to 13, characterised in that a body fluid or a tissue from a cancer patient is treated ex vivo, in particular bone marrow, blood, serum or organ components.
- 17. The use according to claim 16, characterised in that the cancer patient is treated within the frame of a high dosage chemotherapy.
- 18. The use according to claim 16, characterised in that the

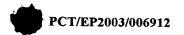
body fluid, or the tissue, respectively, is derived from a patient with the risk of a cancer disease.

- 19. A method of producing a preparation based on a body fluid or tissue, in particular bone marrow, blood, serum or organ components, by
- ex vivo treatment of the body fluid or of the tissue with an antibody directed against a tumor-associated glycosylation for forming a cellular immune complex, and
- optionally separating the immune complex.
- 20. A preparation obtainable by a method according to claim 18 and having a reduced content of receptors from the EGF-receptor family.
- 21. A method of determining the risk of metastasis formation in a cancer patient, by
- providing a sample of a body fluid from a cancer patient,
- contacting said sample with an antibody directed against a tumor-associated glycosylation for forming a cellular immune complex of potentially present tumor cells with said antibody, and
- qualitative and/or quantitative determination of the immune complex in the body fluid as a measure of the metastasis-forming potential.
- 22. A diagnostic agent, containing an antibody directed against a tumor-associated glycosylation in combination with a carrier for separating a cellular immune complex.
- 23. A diagnostic agent containing an antibody directed against a tumor-associated glycosylation in combination with a labelling for determining a cellular immune complex.



- 1. The use of a preparation based on an antibody directed against a tumor-associated glycosylation for preparing a medicament for the prophylactic and/or therapeutic treatment for the reduction or inhibition, respectively, of the growth of tumor cells in a cancer patient.
- 2. The use according to claim 1 for treating a patient in combination with a chemotherapy.
- 3. The used according to claim 1 for treating a chemotherapy-resistance.
- 4. The use according to claim 1 for treating the "minimal residual disease".
- 5. The use according to any one of claims 1 to 4 for inhibiting glycosylated tumor cell receptors.
- 6. The use according to claim 5 for preventing the mitogenic stimulation of a tumor cell by the epidermal growth factor (EGF) and/or by heregulin.
- 7. The use according to any one of claims 1 to 6 for the lysis of tumor cells which express a receptor from the family of the EGF receptors.
- 8. The use according to any one of claims 1 to 7, characterised in that an antibody is directed against Lewis antigens.
- 9. The use according to any one of claims 1 to 8, characterised in that an antibody directed against an aberrant glycosylation is used, like Lewis x-, Lewis b- and Lewis-y-structures, as well as sialyl-Tn, Tn antigen, GloboH, KH1, TF antigen and alpha-1,3-galactosyl epitope.
- 10. The use according to any one of claims 1 to 9, characterised in that the antibody is a monoclonal antibody, in particular a human, humanized, chimeric or murine antibody.





- 11. The use according to any one of claims 1 to 10, characterised in that an antibody having an affinity to binding the EGF receptor with a dissociation constant of below a Kd value of 10⁻⁶ mol/l, preferably less than 10⁻⁷mol/l, most preferred 10⁻⁸mol/l, for less, is used.
- 12. The use according to any one of claims 1 to 11, characterised in that the antibody is used in a dose of at least 50 mg, preferably at least 100 mg, most preferred at least 200 mg, up to 2 g per patient.
- 13. The use according to any one of claims 1 to 12, characterised in that an antibody derivative is used which comprises at least the Fab-portion of an antibody and binds to a tumorassociated glycosylation.
- 14. The use according to any one of claims 1 to 13, characterised in that the patient suffers from a cancer with tumor cells which express a receptor from the family of the EGF receptors.
- 15. A pharmaceutical preparation for treating cancer patients and containing an antibody directed against a tumor-associated glycosylation at a concentration ranging from 0.1-10%, preferably 1-5%.
- 16. A preparation for the pharmaceutical and/or diagnostic use, based on an antibody derivative comprising at least a Fabportion of an antibody which binds to a tumor-associated glycosylation and has a CDC and ADCC activity of less than 50% of the native antibody.
- 17. The use according to any one of claims 1 to 14, characterised in that a body fluid or a tissue from a cancer patient is treated ex vivo, in particular bone marrow, blood, serum or organ components.
- 18. The use according to claim 17, characterised in that the cancer patient is treated within the frame of a high dosage chemotherapy.





- 19. The use according to claim 17, characterised in that the body fluid, or the tissue, respectively, is derived from a patient with the risk of a cancer disease.
- 20. A method of producing a preparation based on a body fluid or tissue, in particular bone marrow, blood, serum or organ components, by
- ex vivo treatment of the body fluid or of the tissue with an antibody directed against a tumor-associated glycosylation for forming a cellular immune complex, and
- optionally separating the immune complex.
- 21. A preparation obtainable by a method according to claim 19 and having a reduced content of receptors from the EGF-receptor family.
- 22. A method of determining the risk of metastasis formation in a cancer patient, by
- providing a sample of a body fluid from a cancer patient,
- contacting said sample with an antibody directed against a tumor-associated glycosylation for forming a cellular immune complex of potentially present tumor cells with said antibody, and
- qualitative and/or quantitative determination of the immune complex in the body fluid as a measure of the metastasis-forming potential.
- 23. A diagnostic agent, containing an antibody directed against a tumor-associated glycosylation in combination with a carrier for separating a cellular immune complex.
- 24. A diagnostic agent containing an antibody directed against a tumor-associated glycosylation in combination with a labelling for determining a cellular immune complex.